REMARKS

Claims 1-59 remain in this application. Claims 40-43 and 50-58 have been amended. Obvious typographical errors have been corrected in claims 40-43. Claims 39, 48, 49 and 59 have been withdrawn as the result of an earlier restriction requirement. Applicant retains the right to present claims 39, 48, 49 and 59 in a divisional application if they are canceled from the present application. Applicant respectfully requests reconsideration in view of the following remarks.

Applicant's Response to Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1-59 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicant respectfully traverses this rejection.

More specifically, the Examiner contends that the term "prodrug" renders the claims indefinite because one skilled in the art cannot say which prodrug is intended. On the contrary, prodrugs are well known in the art to include the inactive pre-cursors of a drug, which are converted into the active form by the body's metabolic processes. The American Heritage Dictionary of the English Language (4th ed. 2000). The pre-cursor will generally include a cleavable hydrolysable moiety such as an ester or amide group. Furthermore, many of such structures are included within the structure of Formula I, and are specifically described in the specification at pages 35-37. Therefore, reconsideration and withdrawal of the rejection is appropriate and respectfully requested.

Applicant's Response to Rejections under 35 U.S.C. §112, First Paragraph

Claims 40-58 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner cites the following reasons: 1) there has never been a compound capable of treating cancers generally; 2) there has never been a compound effective against autoimmune diseases generally; 3) there is no such thing as a broad spectrum anti-viral agent; and 4) a potential infringer would not know what activity reads on

"inhibiting CDK1-CDK-9 activities" as recited in claims 50-58 without extensive experimentation.

These rejections are respectfully traversed.

Enablement as required by the MPEP 2164.04, requires that:

> **A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.**

The enablement requirement also includes that the specification must enable a person of ordinary skill in the art to make and use the invention without undue experimentation. However, "whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims" Id.

The specification of the present invention provides the required disclosure. With respect to the first reason cited by the Examiner, claims 40-43 are not directed to the treatment of cancer generally, but rather to the treatment of cancer associated with CDK activity. As taught by the specification at pages 1-4, cyclin dependent kinases (CDKs) play a role in regulating cellular generation. CDK related malfunctions have been linked to unregulated cellular growth and tumor development. Endogenous inhibitors of CDK have an effect on cellular proliferation because they interact with the CDK complexes. Therefore, cells that are deficient in such

endogenous inhibitors experience cellular proliferation disorders and are prone to tumor formation, which is associated with, for example, cancer. CDK inhibitors, such as those of the present invention, can be useful in treating such cellular proliferation disorders. In view of this, the compounds of the present invention can be useful in treating those cancers that are associated with CDK malfunctions in the body. Even more specifically, the CDK inhibitors of the present invention can be useful in treating a variety of specific types of cancer, as recited in claim 41, as well as specifically inhibiting tumor angiogenesis and metastasis, as recited in claim 43.

In the second reason given by the Examiner, he asserts that there is no compound effective against autoimmune diseases generally. Applicant is not suggesting that the compounds of the present invention are effective against auto-immune diseases generally, but rather those auto-immune diseases associated with CDK activity. Specific auto-immune diseases that can be treated in accordance with the present invention are recited in the specification at page 3, namely, systemic lupus, erythematosus, autoimmune mediated glomerulonephritis, rheumatoid arthritis, psoriasis, inflammatory bowel disease, and autoimmune diabetes mellitus. Claims 40 and 42 have been amended to recite these specific auto-immune diseases.

In the third reason provided by the Examiner, he asserts that there is no such thing as a broad spectrum anti-viral agent. Applicant is not suggesting that the compounds of the present invention act as a broad-spectrum anti-viral agent, but rather a CDK inhibitor effective in treating the specifically listed viral infections in claim 45: HIV, human papilloma virus, herpesvirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus.

The final reason for rejection asserts that claims 50-58 read on patients with various levels of CDK activity, and thereby, require undue experimentation. Applicant has amended claims 50-58 to address this rejection, i.e., removal of the language "in need thereof" as referring to the patient. Claim 50-58 are directed to methods of inhibiting the activity of specific CDKs by administering a compound of the present invention to a patient. This administration will result in

inhibition of CDK in the patient regardless of the level of CDK activity the patient is expressing. Undue experimentation is not required to achieve this result.

With respect to claims 44 and 47, the Examiner has not provided any reasoning for the Section 112, first paragraph rejections.

Considering the arguments provided above, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph are appropriate and respectfully requested.

Applicants' Response to Rejections under 35 U.S.C. §103

Claims 1-59 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over PCT Publication WO 99/54308 to Nugiel et al. (hereinafter "Nugiel"). Applicant respectfully traverses this rejection.

The Examiner contends that Nugiel "teaches a generic group of structurally similar compounds which embraces applicants' claimed compounds." As support, the Examiner refers to pages 5-17 of Nugiel, particularly compounds of formula (I) and definitions of the variables. The Examiner further states that the claims of the present invention differ from Nugiel "by reciting specific species and a more limited genus than the reference." The Examiner contends, however, that it would have been obvious to one skilled in the art to select any species of the genus taught by Nugiel.

Contrary to the Examiner's allegations, however, the compounds claimed in the present invention are not embraced by the genus disclosed in Nugiel, i.e., compounds of formula (I) disclosed at pages 5-17. In particular, the R^1 group in Nugiel's formula (I) does not encompass the compounds of the present invention.

More specifically, the R^1 group in Nugiel's formula (I) corresponds to the -NH-NR^1R^3 moiety in the compounds of the present invention. Although R^1 in Nugiel's formula (I) is

defined to include -NHR^4, and R^4 is defined to include -NR^{3}R^{3a}, the definitions of R^3 and R^{3a} cannot encompass Applicant's claimed compounds. Neither the R^3 nor the R^{3a} group of Nugiel teaches the R^1 group as recited in Applicant's claimed compounds. In particular, Applicant's claims define R^1 as:

> **selected from the groups: C_3-C_{10} membered carbocycle substituted with 0-5 R^4, and 3-10 membered heterocycle substituted with 0-5 R^5, provided that if R^1 is phenyl then R^1 is substituted with 1-5 R^4.**

In contrast, Nugiel's definitions of R^3 and R^{3a} are as follows:

> **R^3 is selected from the group: H, halo, -CN, NO_2, C_{1-4} haloalkyl, NR^5R^{5a}, $NR^5NR^5R^{5a}$, $NR^5C(O)OR^5$, $NR^5C(O)R^5$, =O, OR^5, COR^5, CO_2R^5, $CONR^5R^{5a}$, $NHC(O)NR^5R^{5a}$, $NHC(S)NR^5R^{5a}$, $SO_2NR^5R^{5a}$, SO_2R^{5b}, C_{1-4} alkyl, phenyl, and benzyl;**
>
> **R^{3a} is selected from the group: H, C_{1-4} alkyl, phenyl, and benzyl;**

(Nugiel, at 7).

Nugiel's R^3 and R^{3a} groups do not include a carbocycle or heterocycle as defined above for R^1. The only cyclic groups contained in the Nugiel definitions of R^3 and R^{3a} are phenyl and benzyl, neither of which is substituted. In contrast, Applicant's definition of R^1 includes substituted phenyl, i.e., "if R^1 is phenyl then R^1 is substituted with 1-5R^4." Therefore, Nugiel's compounds do not encompass this group. The only other cyclic group taught by Nugiel is benzyl. Benzyl is a C6H5CH$_2$- radical, in which the linkage to the N atom of the NR^{3}R^{3a} moiety would occur via the CH$_2$- portion. As such, benzyl is not a carbocycle, which may optionally be substituted, as defined by Applicant and recited in the definition of R^1. In view of this, Nugiel's R^3 and R^{3a} groups cannot encompass Applicant's claimed compounds.

Therefore, Nugiel's compounds of formula (I) do not embrace, and are distinctly different from, Applicant's claimed compounds. Applicant's compounds are not a species that can be selected from the genus taught by Nugiel. Because Applicant's compounds are not disclosed, taught or suggested by Nugiel, reconsideration and withdrawal of the Section 103 rejection is respectfully requested.

Applicant's Response to Double Patenting Rejection

The Examiner has rejected claim 1 under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-57 of U.S. Patent No. 6,407,103 (hereinafter "the '103 Patent") and claims 1-4 of U.S. Patent No. 6,593,356 (hereinafter "the '356 Patent"). Applicant respectfully traverses the rejections.

The '103 Patent claims priority to the same U.S. Provisional Application (60/082,476) as the Nugiel reference, discussed in the response to the Section 103 rejection above. Accordingly, the compounds of formula (I) contained in claims 1-57 of the '103 Patent similarly do not encompass the compounds claimed in the present invention. The compounds of the '103 Patent do not encompass, and recite a distinctly different definition of, the R^1 group defined in Applicant's claim 1, as discussed in detail above. As such, claim 1 is not "embraced by the patented claims," as suggested by the Examiner, and the obviousness-type double patenting rejection should be withdrawn.

The '356 Patent similarly fails to embrace the compounds of claim 1. As above, the R^3 and R^{3a} groups of the '356 Patent fail to encompass the R^1 group defined in the present invention. In the '356 Patent, R^{3a} is defined as "H or C_{1-4} alkyl" whereas R^3 is COR^5. Neither of these groups is a carbocycle or heterocycle as defined by R^1 in Applicant's claim 1. Therefore, claim 1 is not embraced by, and is distinctly different from, the claims of the '356 Patent. In view of this, Applicant respectfully requests reconsideration and withdrawal of the obviousness-type double patenting rejection.

Accordingly, Applicant believes the present claims to be in condition for allowance and respectfully requests withdrawal of the rejections.

Should the Examiner have any questions, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number set forth below.

Respectfully submitted,

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